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PRINCIPAL INVESTIGATOR: Susan Raatz, Ph.D., R.D.

CONTRACTING ORGANIZATION: University of Minnesota
Minneapolis, MN 55455

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Susan Raatz, Ph.D., R.D.

E-Mail: raatz001@umn.edu

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14. ABSTRACT

Epidemiological and animal studies associate high levels of dietary fat with increased risk of sex hormone mediated cancer, such as breast cancer. A high intake of total fat and omega-6 fatty acids increases risk while omega-3 (n3) fatty acids are associated with risk reduction. Our proposal is testing the effect of dietary fat and fatty acids on sex hormone concentrations in post-menopausal women. The objectives are to evaluate 1) the effects of total fat and n3 intake on plasma and urinary sex hormone levels, 2) the relationship between plasma fatty acids and plasma and urinary sex hormones, and 3) the effects of total fat and n3 on the association between sex hormone concentrations and urinary prostaglandin E_2 (PGE_2). We are performing a randomized, Latin square-designed controlled feeding study testing High Fat, Low Fat, and Low Fat + n3 diets, each of 8 week duration. In order to determine the estrogenic effects of the diets, sex hormone endpoints will be measured reflecting availability, metabolism, and action. Plasma fatty acids fractions and urinary PGE_2 will be measured to evaluate mechanistic effects. At present 139 women have been screened by telephone, 24have been screened in the clinic, 24have been enrolled in the trial. Sixteen subjects have completed all aspects of the trial. Preliminary data of the sex hormone samples for the first 10 subjects has resulted in 2 abstracts for presentation at the DOD 2008 Era of Hope meeting. No manuscripts have yet been generated.

dietary fat, omega-3 fatty acids, eicosanoids, sex hormones

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Introduction

Our project addresses important questions about the effects of dietary total fat and fatty acids on sex hormone concentrations in postmenopausal women. The study is being conducted at the General Clinical Research Center of the University of Minnesota. Our guiding hypothesis is that dietary total fat and fatty acid content affect sex hormone concentrations in a manner associated with sex hormone mediated cancer risk. The specific objectives are 1) to evaluate the effects of total fat and omega-3 fatty acid intake on plasma and urinary sex hormone levels in postmenopausal women, 2) to evaluate the relationship between plasma concentrations of specific fatty acids and concentrations of plasma and urinary sex hormones, and 3) to evaluate the effects of total fat and omega-3 fatty acids on the association between sex hormone concentrations and urinary prostaglandin E_2 and thromboxane B_2 concentrations.

We are conducting a well controlled feeding study to evaluate the role of fat and fatty acids in 24 healthy, postmenopausal women. The diets being tested include a "high risk" American diet (40% fat), a low fat diet (20% fat) and a low fat diet with supplemental omega-3 fatty acids (23% fat). Endpoints are being measured to assess availability, metabolism, and action of sex hormones in response to the diets. Plasma fatty acids fractions and urinary prostaglandin E_2 is being measured to evaluate mechanistic effects of dietary fat.

Increased understanding of the mechanisms by which dietary fat affect sex hormone action may provide critical information for the development of cancer-preventative dietary recommendations. Nutrition information provided as focused guidelines regarding fat intake can be developed for public use that indicate which types of foods to include in the daily diet and which to avoid.

Body

Study Progress:

The project is proceeding along the time line as defined in our statement of work. We received final approval to initiate the project from the University of Minnesota Human Subject Protection Program/Internal Review Board on 10/29/2004. A no-cost extension has been granted for 1 year through 4/30/10.

Extensive recruitment efforts are ongoing. We advertise throughout the medical campus and surrounding campus buildings and through a text ad in the Fairview University Medical Center staff and patient flier. A total of 139 subjects have been screened by telephone, 24 subjects have been screened at the research center and 24 subjects have completed the feeding trial. The final subject will completed the feeding portion of the trial in January 09. Analysis of the remaining hormones, Eicosanoids and fatty acids are currently being completed.

Personnel:

The following personnel were supported on this grant
Susan Raatz PhD RD, Principle Investigator (5% effort)
Mindy Kurzer PhD, Co-investigator (5% effort)
J Bruce Redmon MD, Co-investigator (5% effort)
Michael Walcher, Senior Scientist (25% effort)
Natalie Hansen, Student Food Service Worker (75% effort)

Lindsay Orr BA, Graduate Research Assistant – Currently funded on a DOD Predoctoral Fellowship based on this project

Key Research Accomplishments

Plasma sex hormone analysis for all subjects has been completed. These data showed a trend for decreased concentrations from baseline to 8 weeks for estradiol with the low fat and low fat-high n-3 diets. Consumption of the low fat-high n-3 diet increased sex hormone binding globulin concentrations significantly from baseline to 8 weeks ($p = 0.04$). The calculated estrogen index showed a trend for increase from baseline to 8 weeks in the high fat compared to the low fat high-n-3 diet at week 8 ($p = .08$). The calculated androgen index was significantly increased following the high fat compared to low fat and low fat-high n-3 diet ($p = .006$ and .002, respectively).

Preliminary data shows that within subjects, 8 weeks consumption of a low fat-high n-3 diet significantly decreased plasma estradiol and increased sex hormone binding globulin concentrations in postmenopausal women. Compared to high fat diet, consumption of the low fat and low fat-high n-3 diets significantly decreased estradiol concentrations between groups at 8 weeks. The high fat diet resulted in a increased androgen and estrogen index.

Reportable Outcomes

Training:

Lindsay Orr, BA, a graduate student in Human Nutrition, received a DOD Breast Cancer Research Program predoctoral traineeship award (Award #W81XWH-06-1-0778) in August of 2006 based on this study. This grant will continue ctober 2009. At that time her effort for completion of the graduate program will be transferred to this grant.

Data Presentation:

Two abstracts were presented at the 2008 Era of Hope meeting as both posters and platform presentation:

Breast cancer risk reduction: Effect of dietary fat and fatty acids on plasma estrogen and testosterone indices in postmenopausal women SK Raatz[1,2], NK Hanson[2], LR Orr[2], JB Redmon[1], MS Kurzer[2] Departments of [1]Medicine and [2]Food Science and Nutrition, University of Minnesota, Minneapolis, MN

Effect of High Omega-3 Fatty Acid Diet on Markers of Breast Cancer Risk in Postmenopausal Women Orr L.R.[2], Redmon J.B.[1], Kurzer M.S.[2], Raatz S.K.[1] Departments of [1]Medicine and [2]Food Science and Nutrition, University of Minnesota, Minneapolis, MN

Conclusions

The study is progressing as projected on the "Statement of Work". Given the nature of a long term feeding trial, no reportable data has yet been obtained. All of the participants have completed the clinical components of the study and laboratory analysis

is being completed for the urinary sex hormones, eicosanoids, and fatty acids. The study progress is as expected with recruitment of participants proceeding smoothly. The test diets are well accepted by the participants, all endpoint visits have gone well.

We expect to generate 3 primary papers from this project:

1. Primary results – Effect of fat modified diets on plasma sex hormone concentrations
2. Secondary results - Effect of fat modified diets on urinary sex hormone metabolite concentrations
3. Secondary results - Effect of fat modified diets on urinary eicosanoids and plasma fatty acids

References

None